REMARKS

Claims 1, 4-18, 84, and 97-225, are pending in the present application. Claims 4, 15-18, 102, 108-127, 143-147, 149-151, 154-181, 184-188, 191-195, 198-202, 205, 208, 212-216, 220-221, and 224 were previously withdrawn from consideration as drawn to a non-elected invention. By virtue of this response, claims 99, 109, 118, 129, 133, 138, 142, 219, 222-223, and 225 have been canceled, and claims 1, 5-6, 84, 97, 103, 128, 130-131, 134, 137, 139-140, 148, 152-153, 209, and 217-218 have been amended. Accordingly, claims 1, 5-14, 84, 97-98, 100-101, 103-107, 128, 130-132, 134-137, 139-141, 148, 152-153, 182-183, 189-190, 196-197, 203-204, 206-207, 209-211, and 217-218 are currently under consideration.

Amendments

Claims 1, 5-6, 84, 97, 103, 128, 130-131, 134, 137, 139-140, 148, 152-153, 209, and 217-218 have been amended. Support for the amendments of claims 84, 128, and 137 are found, for example, in paragraphs [0018] and [0041] of the specification. Support for the amendments of claims 148 and 152-153 are found, for example, in paragraphs [0033], [0051], [0053], [0064], [0156], and [0159] of the specification. Support for the amendments of claims 1, 5-6, 97, 103, 130-131, 139-140, 209, and 217-218 are found, for example, in paragraph [0018] of the specification. Claim 134 was amended to address a typographical error.

With respect to all amendment to claims, Applicants have not dedicated or abandoned any unclaimed subject matter and, moreover, have not acquiesced to any rejections and/or objections made by the Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation, continuation-in-part, and/or divisional applications.

Claim Rejections – 35 USC § 112, first paragraph

A. Claims 1, 84, 103, 105, and 107, and their dependent claims stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully traverse.

The Examiner alleges that the specification while being enabled for an effective amount of human serum albumin to reduce one or more side effects of a pharmaceutical agent in a human, does not reasonably provide enablement for an effective amount of albumin from any source and/or species to reduce one or more side effects of a pharmaceutical agent in a human. *See* Office Action dated 04/24/08 at page 2.

Applicants respectfully disagree. Without acquiescing to the correctness of the Examiner's remarks and solely to expedite prosecution, Applicants have amended claims 1, 84, 103, 105, and 107 to recite "human serum albumin."

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the enablement rejections of claims 1, 84, 103, 105, and 107 under 35 U.S.C. § 112, first paragraph.

B. Claims 1, 84, 103, 105, and 107, and their dependent claims stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Applicants respectfully traverse.

The Examiner alleges that the skilled artisan cannot envision all different sources of albumin protein and their amounts effective to reduce one or more side effects in humans, but acknowledges that the specification describes human serum albumin. *See* Office Action dated 04/24/08 at page 5.

Applicants respectfully disagree. Without acquiescing to the correctness of the Examiner's remarks and solely to expedite prosecution, Applicants have amended claims 1, 84, 103, 105, and 107 to recite "human serum albumin."

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the written description rejections of claims 1, 84, 103, 105, and 107 under 35 U.S.C. § 112, first paragraph.

Claim Rejections – 35 USC § 112, second paragraph

Claims 1, 5-14, 84, 97-101, 103-107, 128-142, 148, 152-153, 182-183, 189-190, 196-197, 203-204, 206-207, 209-211, 217-219, 222-223, and 225, stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Applicants respectfully traverse.

Claims 1, 84, 103, 105, and 107

The Examiner alleges that claims 1, 84, 103, 105, and 107 and their dependent claims are indefinite as the claims are drawn to a pharmaceutical composition comprising a pharmaceutical agent and a pharmaceutical acceptable carrier, but the claims appear to regard both albumin and deferoxamine as pharmaceutical carriers. *See* Office Action dated 04/24/08 at page 6. The Examiner states that the composition must comprise more than one carrier or one of the constituents should be deleted and further clarification is requested. *See id.*

Applicants respectfully disagree. Without acquiescing to the correctness of the Examiner's remarks and solely to expedite prosecution, Applicants have amended the claims 1 and 84 to clarify that the pharmaceutical composition comprises a pharmaceutically acceptable carrier, wherein the pharmaceutically acceptable carrier comprises human serum albumin and the pharmaceutical composition further comprises deferoxamine.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1, 84, 103, 105, and 107 under 35 U.S.C. § 112, second paragraph.

Claims 1 and 134

The Examiner alleges that claims 1 and 134 are indefinite as reciting improper Markush language. *See* Office Action dated 04/24/08 at page 6.

Applicants have amended claims 1 and 134, per the Examiner's suggestion, to add the term "and" before "mycophenolic acids." Applicants submit that the rejection in view of the amendments is obviated.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1 and 134 under 35 U.S.C. § 112, second paragraph.

Claims 84, 128-129, and 137-138

The Examiner further alleges claims 84, 128-129, and 137-138 are indefinite as the claims recite a ratio of albumin to a pharmaceutical agent is about 18:1, 15:1, or 9:1 or less, which,

according to the Examiner, comprises a weight ratio of albumin to pharmaceutical agent which is 0 to 0. *See* Office Action dated 04/24/08 at page 6.

Applicants respectfully disagree. The metes and bounds of the claims are clearly defined. Applicants respectfully note that the Examiner's interpretation of the claims to include no pharmaceutical agent and no protein results in no claimed composition.

Without acquiescing to the correctness of the Examiner's remarks and solely to expedite prosecution, Applicants have amended claims 84, 128, and 137 as indicated herein to recite a lower ratio limit. Applicants note that claims 129 and 138 have been canceled.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 84, 128, and 137 under 35 U.S.C. § 112, second paragraph.

Claims 148 and 152-153

The Examiner alleges that claims 148 and 152-153 are indefinite because there is no lower limit to the nanoparticle's mean size and the size could be 0 nm. *See* Office Action dated 04/24/08 at page 6.

Applicants respectfully disagree. Applicants submit that the metes and bounds of the claims are clearly defined as set forth and note that the interpretation of the particle size to include 0 nm would render recitation of a nanoparticle meaningless.

In *In re Kirsch*, 498 F.2d 1389, 182 USPQ 286 (CCPA 1974), a claim limitation required that the amount of one ingredient in the reaction mixture should "be maintained at less than 7 mole percent." *See also* MPEP § 2173.05(d). "The Examiner argued that the claim was indefinite because the limitation sets only a maximum amount and is inclusive of substantially no ingredient resulting in termination of any reaction." MPEP § 2173.05(d). The court, however, found no merit in the Examiner's rejection, because the claim was clearly directed to a process which "did not warrant distorting the overall meaning of the claim to preclude performing the claimed process." MPEP § 2173.05(d).

Similarly in the present application, claims 148 and 152-153 depend from a claim directed to a pharmaceutical composition, wherein the albumin and the pharmaceutical agent are formulated as

nanoparticles. If claims 148 and 152-153 encompassed 0 nm, the interpretation would distort the overall meaning of the claim to preclude nanoparticles. As such, in view of *In re Kirsch*, as discussed above, dependent claims 148 and 152-153 are definite and does not encompass non-nanoparticles, 0 nm.

Further, the Examiner alleges that the term "mean size" is unclear. *See* Office Action dated 04/24/08 at page 6. Without acquiescing to the correctness of the Examiner's remarks and solely to expedite prosecution, Applicants have amended claims 148 and 152-153 to recite "mean diameter."

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 148 and 152-153 under 35 U.S.C. § 112, second paragraph.

In view of the arguments presented above, Applicants respectfully request reconsideration and withdrawal of all the rejections to claims 1, 5-14, 84, 97-101, 103-107, 128-142, 148, 152-153, 182-183, 189-190, 196-197, 203-204, 206-207, 209-211, 217-219, 222-223, and 225 under 35 U.S.C. § 112, second paragraph.

Claim Rejections – 35 USC § 102(b)

A. Yang et al. (1993 Biochemical Pharmacology 46(2): 336-339)

Claims 84, 128-129, and 132-133, stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Yang et al. (1993 *Biochemical Pharmacology* 46(2): 336-339). Applicants respectfully traverse.

As a preliminary matter, Applicants respectfully note that claim 84 has been amended to recite "wherein the weight ratio of albumin to pharmaceutical agent is about 1:1 to about 18:1."

The Examiner states that Yang et al. "teach a composition comprising human serum albumin, dihydroartemisinin, and deferoxamine (DFO, 1 mM)…" and cites page 336, column 2 of Yang et al. *See* Office Action dated 04/24/08 at page 7.

Applicants submit that Yang et al. disclose studies regarding the interaction between artemisinin and human serum in vitro using [^{3}H]-dihydroartemisinin and [^{14}C]-artemisinin. *See* Yang et al. at page 336. Applicants note that Yang et al. do not disclose a pharmaceutical composition comprising deferoxamine. Further, Yang et al. do not disclose a pharmaceutical

composition comprising a weight ratio of albumin to pharmaceutical agent is about 1:1 to about 18:1 as recited in independent claim 84. Claims 128-129 and 132-133 depend from independent claim 84.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 84, 128-129, and 132-133 under 35 U.S.C. § 102(b) as allegedly being anticipated by Yang et al. (1993 *Biochemical Pharmacology* 46(2): 336-339).

B. Ritov et al. (2001 Diabetes 50: 1253-1262)

Claims 84, 128-129, and 132, stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Ritov et al. (2001 *Diabetes* 50: 1253-1262). Applicants respectfully traverse.

The Examiner states that Ritov et al. "teach a composition comprising 100 mmol/l mannitol, 5.0 mg/ml bovine serum albumin (BSA), 100 umol/l deferoxamine mesylate, 20 umol/l leupeptide, etc." and cites page 1254, column 1 of Ritov et al. *See* Office Action dated 04/24/08 at page 7.

Applicants submit that Ritov et al. disclose studies related to the activity and subcellular distribution of hexokinase isozymes in human skeletal muscles. *See* Ritov et al at page 1253. Applicants note that the composition in Ritov et al. discussed by the Examiner is a homogenization medium for separation of hexokinase, not a pharmaceutical composition as required in claims 84, 128-129, and 132. Further, there is no pharmaceutical agent disclosed in the homogenization medium. *See* Ritov et al. at page 1254, column 1. Ritov et al. also do not teach a pharmaceutical composition comprising a weight ratio of albumin to pharmaceutical agent is about 1:1 to about 18:1 as recited in independent claim 84. Claims 128-129 and 132 depend from independent claim 84.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 84, 128-129, and 132 under 35 U.S.C. § 102(b) as allegedly being anticipated by Ritov et al. (2001 *Diabetes* 50: 1253-1262).

C. Meijs et al. (1996 Nuclear Medicine & Biology 23: 439-448)

Claims 84, 128-129, and 132, stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Meijs et al. (1996 *Nuclear Medicine & Biology* 23: 439-448). Applicants respectfully traverse.

The Examiner states that Meijs et al. teach a composition comprising BSA and desferal (Df)…" and cites page 440, column 1.

Applicants submit that Meijis et al. disclose a method to label proteins with zirconium (Zr)-isotopes. *See* Meijis et al. at page 439. Applicants note that Meijis et al. do not teach a pharmaceutical composition comprising a weight ratio of albumin to pharmaceutical agent is about 1:1 to about 18:1 as recited in independent claim 84. Claims 128-129 and 132 depend from independent claim 84.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 84, 128-129, and 132 under 35 U.S.C. § 102(b) as allegedly being anticipated by Meijs et al. (1996 *Nuclear Medicine & Biology* 23: 439-448).

D. Klebanoff et al. (1989 Journal of Biol Chem 264(33): 19765-19771)

Claims 84, 128-129, and 132-133, stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Klebanoff et al. (1989 *Journal of Biol Chem* 264(33): 19765-19771). Applicants respectfully traverse.

The Examiner states that Klebanoff et al. "teach a mixture comprising 8 $x10^{-6}$ M sodium iodide (4000 pmol), 0.2 mg/mL human albumin, and deferoxamine…." And cites page 19768 of Klebanoff et al. *See* Office Action dated 04/24/08 at page 8.

Applicants submit that Klebanoff et al. disclose that deferoxamine can "increase iron-dependent radical formation with potentiation of toxicity to microorganisms." Klebanoff et al. at page 19765. Applicants note that Klebanoff et al., however, do not teach a pharmaceutical composition. Further, Klebanoff et al. do not teach a weight ratio, wherein the weight ratio of albumin to pharmaceutical agent is about 1:1 to about 18:1 as recited in independent claim 84. Claims 128-129 and 132-133 depend from independent claim 84.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claim 84, 128-129, and 132-133 under 35 U.S.C. § 102(b) as allegedly being anticipated by Klebanoff et al. (1989 *Journal of Biol Chem* 264(33): 19765-19771).

E. Gutteridge et al. (1981 Journal of Inorganic Biochemistry 15: 349 357)

Claims 84, 128-129, 132, and 182-183, stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Gutteridge et al. (1981 *Journal of Inorganic Biochemistry* 15: 349-357). Applicants respectfully traverse.

The Examiner stated that Gutteridge et al. "teach a composition comprising bleomycin, ferrous ions, and desferrioxamine" and cites page 353 of Gutteridge et al. *See* Office Action dated 04/24/08 at page 8-9.

Applicants submit that Gutteridge et al. disclose that studies related to iron-dioxygen-dependent damage to the bleomycin complex. Gutteridge et al. at page 350. Applicants note that Gutteridge et al. do not, however, teach a pharmaceutical composition and, in particular, a pharmaceutical composition comprising a weight ratio of albumin to pharmaceutical agent is about 1:1 to about 18:1 as recited in independent claim 84. Claims 128-129, 132, and 182-183 depend from independent claim 84.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 84, 128-129, 132, and 182-183 under 35 U.S.C. § 102(b) as allegedly being anticipated by Gutteridge et al. (1981 *Journal of Inorganic Biochemistry* 15: 349-357).

F. Gutteridge (1984 Biochemical Pharmacology 33(19): 3059-3062)

Claims 84, 128-129, 132, and 182-183, stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Gutteridge (1984 *Biochemical Pharmacology* 33(19): 3059-3062). Applicants respectfully traverse.

The Examiner stated that Gutteridge "teaches a composition comprising streptonigrin, deoxyribose, and desferrioxamine" and cites page 3061 Table 2 of Gutteridge. *See* Office Action dated 04/24/08 at page 9.

Applicants submit that Gutteridge discloses that "deoxyribose degradation under conditions of low oxygen concentration is inhibited by superoxide dismutase." Gutteridge at page 3059. Applicants note that Gutteridge does not, however, teach a pharmaceutical composition and, specifically, a pharmaceutical composition comprising a weight ratio of albumin to pharmaceutical agent is about 1:1 to about 18:1 as recited in independent claim 84. Claims 128-129, 132, and 182-183 depend from independent claim 84.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 84, 128-129, 132, and 182-183 under 35 U.S.C. § 102(b) as allegedly being anticipated by Gutteridge (1984 *Biochemical Pharmacology* 33(19): 3059-3062).

Claim Rejections – 35 USC § 103(a)

A. Yang et al. (1993 Biochem. Pharm. 46(2): 336-339) in view of current pharmaceutical practice

Claims 103 and 104 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Yang et al. (1993 *Biochem. Pharm.* 46(2): 336-339) in view of current pharmaceutical practice. Applicants respectfully traverse.

The Examiner alleges that it would have been obvious to one of ordinary skill in the art to "lyophilize the composition of Yang et al. because one of ordinary skill would recognize that the components of the composition would remain the same lyophilizing said composition would create a stable product for storage...." *See* Office Action dated 04/24/08 at page 10. The Examiner also states that Yang et al. "teach the composition comprising human serum albumin, dihydroartemisinin, and deferoxamine comprises human serum and Tris buffer in a 1:4 v/v (p. 336)" and concludes that "the composition of Yang et al. meets the limitation of 25% by weight of albumin (claim 103). *See id.*

Applicants respectfully disagree. Applicants respectfully note that Yang et al. disclose mixing human serum, not human serum albumin, with 4 volumes of Tris buffer. Further, as discussed above, Yang et al. do not disclose a pharmaceutical composition. Yang et al. also do not teach or suggest a pharmaceutical composition comprising a weight ratio of albumin to

pharmaceutical agent is about 1:1 to about 18:1 as recited in the claims. Yang et al. also does not teach or suggest lyophilized or dehydrated pharmaceutical composition.

The current pharmaceutical practice does not cure the deficiencies of Yang et al. Specifically the current pharmaceutical practice is relied on only as to methods to dehydrate and/or lyophilize to create a stabile product for storage and/or reconstitution. *See* Office Action dated 04/24/08 at page 10.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 103 and 104 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Yang et al. (1993 *Biochem. Pharm.* 46(2): 336-339) in view of current pharmaceutical practice.

B. Ritov et al. (2001 Diabetes 50: 1253-1262) in view of current pharmaceutical practice

Claims 105, 106, and 209, stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ritov et al. (2001 *Diabetes* 50: 1253-1262) in view of current pharmaceutical practice. Applicants respectfully traverse.

The Examiner alleges that it would have been obvious to one of ordinary skill in the art "to lyophilize the composition of Ritov et al. because one of ordinary skill would recognize that the components of the composition would remain the same lyophilizing said composition would create a stable product for storage …." *See* Office Action dated 04/24/08 at page 11. The Examiner further states Ritov et al teach a composition comprising 100 mmol/l mannitol, 5.0 mg/ml bovine serum albumin (BSA), 100 umol/l deferoxamine mesylate, 20 umol/l leupeptide, etc." *See* Office Action dated 04/24/08 at page 10.

Applicants respectfully disagree. As discussed above, Ritov et al. disclose a homogenization medium, not a pharmaceutical composition as required in claims 105, 106, and 209. Further, there is no pharmaceutical agent disclosed in the homogenization medium. Ritov et al. do not teach or suggest a pharmaceutical composition comprising a weight ratio of albumin to pharmaceutical agent is about 1:1 to about 18:1.

The current pharmaceutical practice does not cure the deficiencies of Ritov et al. Specifically the current pharmaceutical practice is relied on only as to methods to dehydrate and/or

lyophilize to create a stabile product for storage and/or reconstitution. *See* Office Action dated 04/24/08 at page 11.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 105, 106, and 209 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Ritov et al. (2001 *Diabetes* 50: 1253-1262) in view of current pharmaceutical practice.

C. Gutteridge et al. (1981 Journal of Inorganic Biochemistry 15: 349-357) in view of current pharmaceutical practice

Claims 107, 131, and 152 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Gutteridge et al. (1981 *Journal of Inorganic Biochemistry* 15: 349-357) in view of current pharmaceutical practice. Applicants respectfully traverse.

The Examiner alleges that it would have been obvious to one of ordinary skill in the art "to manufacture the composition of Gutteridge, which comprises bleomycin, ferrous ions, and desferrioxamine, into different formulations, i.e. emulsions, nanoparticles...." *See* Office Action dated 04/24/08 at page 11.

Applicants respectfully disagree. As discussed above, Gutteridge et al. do not teach or suggest a pharmaceutical composition and, in particular, a pharmaceutical composition comprising a weight ratio of albumin to pharmaceutical agent is about 1:1 to about 18:1. Further, Gutteridge et al. do not teach or suggest the pharmaceutical composition described above, wherein the pharmaceutical composition is an oil-in-water emulsion, the albumin and the pharmaceutical agent in the composition are formulated as nanoparticles, or the nanoparticles have a mean size of less than about 200 nm.

The current pharmaceutical practice does not cure the deficiencies of Gutteridge et al. Specifically the current pharmaceutical practice is relied on only as to methods to formulate into different physical forms depending on the route of administration, i.e. capsules, tablets, solutions, oil-in-water emulsions, nanoparticles, etc. *See* Office Action dated 04/24/08 at page 11.

In view of the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 107, 131, and 152 under 35 U.S.C. § 103(a) as allegedly being unpatentable

over Gutteridge et al. (1981 *Journal of Inorganic Biochemistry* 15: 349-357) in view of current pharmaceutical practice.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 638772000300. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: October 24, 2008

Respectfully submitted,

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